

The following listing of claims shall replace all listings and versions previously presented in this application.

**Listing of Claims:**

1. (original) An antibody Fab fragment comprising a heavy chain constant region that terminates at the interchain cysteine of C<sub>H</sub>1.
2. (original) The antibody Fab fragment of claim 1 wherein the interchain cysteine of C<sub>H</sub>1 is covalently linked to the interchain cysteine of C<sub>L</sub>.
3. (currently amended) The antibody Fab fragment of claim 1 wherein the interchain cysteine of C<sub>H</sub>1 is at position 233 of the heavy chain, according to the Kabat numbering system.
4. (currently amended) The antibody Fab fragment of claim 1 wherein the interchain cysteine of C<sub>H</sub>1 is at position 127 of the heavy chain, according to the Kabat numbering system.
5. (currently amended) The antibody Fab fragment of claim 1 wherein the interchain cysteine of C<sub>H</sub>1 is at position 128 of the heavy chain, according to the Kabat numbering system.
6. (currently amended) The antibody Fab fragment of claim 1 wherein the interchain cysteine of C<sub>H</sub>1 is at position 235 of the heavy chain, according to the Kabat numbering system.
7. (currently amended) The antibody Fab fragment of claim 1 wherein the interchain cysteine of the light chain constant region is at position 214 of the light chain, according to the Kabat numbering system.
8. (cancelled)

9. (cancelled)

10. (cancelled).

11. (cancelled)

12. (original) The antibody Fab fragment of claim 1 that has been modified by attachment of one or more effector molecules.

13. (original) The antibody Fab fragment of claim 12 that has been modified by attachment of two or more effector molecules.

14. (original) The antibody fragment of claim 13 wherein an effector molecule is attached to a cysteine in the light chain constant region and to a cysteine in the heavy chain constant region.

15. (original) The antibody fragment of claim 14 wherein the cysteine residues in the heavy and light chain constant regions that are attached to effector molecules would otherwise be linked to each other via a disulphide bond if the effector molecules were not attached.

16. (original) The antibody fragment of claim 15 wherein the light chain cysteine to which an effector molecule is attached is the interchain cysteine of  $C_L$  and the heavy chain cysteine to which an effector molecule is attached is the interchain cysteine of  $C_{H1}$ .

17. (original) The antibody Fab fragment of claim 12 wherein the effector molecule is PEG.

18. (withdrawn) A method of producing the antibody Fab fragment of claim 12 comprising: a. treating an antibody Fab fragment comprising a heavy chain constant region that terminates at the interchain cysteine of  $C_{H1}$  with a reducing agent capable of

generating a free thiol group in a cysteine of the heavy and light chain constant regions of the fragment; and b. reacting the treated fragment with an effector molecule.

19. (withdrawn) The method of claim 18 wherein the reducing agent is a non-thiol based reducing agent.

20. (withdrawn) The method of claim 19 wherein the reducing agent is a trialkylphosphine.

21. (withdrawn) The method of claim 19 wherein the non-thiol based reducing agent is tris(2-carboxyethyl)phosphine (TCEP).

22. (withdrawn) The method of claim 19 wherein the non-thiol based reducing agent is tris(3-hydroxypropyl)phosphine (THP).

23. (withdrawn) The method of claim 18 wherein either or both of steps (a) and (b) are performed in the presence of a chelating agent.

24. (withdrawn) The method of claim 23 wherein the chelating agent is EDTA.

25. (withdrawn) The method of claim 24 wherein both steps (a) and (b) are performed in the presence of EDTA.

26. (original) A composition comprising a mixture of two or more antibody Fab fragments wherein the mixture is enriched for Fab fragments in which the C<sub>H</sub>1 domain terminates at the interchain cysteine, the heavy chains in the fragments are not covalently bonded to the light chains, and the fragments have an effector molecule attached to a cysteine in the light chain constant region and the heavy chain constant region of the fragments.

27. (original) The composition of claim 26 wherein greater than 50% of the mixture

comprises Fab fragments in which the C<sub>H</sub>1 domains terminate at the interchain cysteines, the heavy chains in the fragments are not covalently bonded to the light chains, and the fragments have an effector molecule attached to a cysteine in the light chain constant region and the heavy chain constant region of the fragments.

28. (withdrawn) An isolated DNA sequence encoding the heavy and/or light chain constant regions of the antibody Fab fragment of claim 1.

29. (withdrawn) A cloning or expression vector comprising the isolated DNA sequence of claim 28.

30. (withdrawn) The vector of claim 29, wherein the vector comprises the sequence of SEQ ID NO:5.

31. (withdrawn) The vector of claim 30 further comprising the sequence of SEQ ID NO:6.

32. (withdrawn) The vector of claim 29, wherein the vector comprises the sequence of SEQ ID NO:7.

33. (withdrawn) The vector of claim 32 further comprising the sequence of SEQ ID NO:8.

34. (withdrawn) A host cell expressing the antibody Fab fragment of claim 1.

35. (withdrawn) The host cell of claim 34 comprising the cloning or expression vector of claim 29.

36. (withdrawn) A process for producing the antibody Fab fragment of claim 1 comprising culturing a host cell that expresses an antibody Fab fragment comprising a heavy chain constant region that terminates at the interchain cysteine of C<sub>H</sub>1 and isolating

said fragment.

37. (currently amended) A ~~pharmaceutical~~ composition comprising an antibody Fab fragment of claim 1, together with one or more pharmaceutically acceptable excipients, diluents or carriers.